Remarks

Claims 1-33 are pending. Claims 1, 6, 11-19, 21-27 and 30-32 are cancelled. Claims 1-10, 20, 28, 29, 32 and 33 are rejected. The rejections with regard to cancelled Claims 1, 6 and 32 are now moot. Claims 2-5, 7-10, 20, 28, 29 and 33 are currently amended. The amendments are merely made for the sake of clarity. Claims 34 and 35 are new. Support for the new claims can be found at paragraphs [0014], [0035]-[0048], [0059], [0069], [0071], [0080] and [0084] as well as the claims of the originally filed application.

At the outset, the Applicants wish to thank the Examiner for the helpful interview of June 15, 2009 in which the rejections under 35 USC §112 and 35 USC §103 were discussed. The Applicants note that the amendments, new claims and remarks in the Response are consistent with the helpful guidance provided by the Examiner both during the interview and in the Official Action. The Applicants also thank the Examiner for withdrawing all of the rejections previously made under 35 USC §101.

Claims 7 and 8 are rejected as indefinite under 35 USC §112, second paragraph.

Amended Claims 7 and 8 are definite under 35 USC §112, second paragraph. Claims 7 and 8 are dependent on independent Claim 34 and incorporate all the recitations of this claim. Claim 34 is consistent with the Examiner's guidance during the interview and does not recite "the other cases[,]" "this matrix" or "B_2" as discussed during the interview. Thus, Claims 7 and 8 no longer recite "the other cases[,]" "this matrix" or "B_2" and are definite under 35 USC §112, second paragraph.

The Applicants respectfully request the withdrawal of the rejections of the claims as indefinite under 35 USC §112, second paragraph.

Claims 7 and 8 are rejected as non-enabled under 35 USC §112, first paragraph.

Amended Claims 7 and 8 are enabled under 35 USC §112, first paragraph. As discussed during the interview and described in the Declaration of Ms. Brouillet, one of ordinary skill in the art is enabled to create matrices B and C of the claims without undue experimentation.

For example, as discussed during the interview, one of ordinary skill in the art can determine from Example 1 and the other disclosure in the application how matrices B and C are constructed. In particular, one of ordinary skill in the art would understand from the recitation of "$A_{i,j}=A_{k,j}$....irrespective of the value of j ranging from 0 to N" in paragraphs [0043] and [0047] of the originally filed application and the values in the matrices of Example 1 that a comparison

is made of all the values of each position in two columns of matrix A to supply the values in the B and C matrices. This is because the positions are the columns of matrix A identified by "i" (*e.g.*, POS 0, POS 1, *etc.*) and each cell in the columns in this matrix contains a value for each unique sequence included in the matrix A analysis (recall each unique sequence is identified by a marker value "j" such as SEQ 1, SEQ 2, *etc.*). Thus, "irrespective of the value of j ranging from 0 to N" in reference to "$A_{i,j}=A_{k,j}$" tells one to perform the indicated operations for each value in the column (*e.g.*, for SEQ 1, SEQ 2, *etc.*) because "j" is a marker value which has values ranging from 0 to N in each position column. This is also apparent when one of ordinary skill in the art refers to the Examples.

The Applicants respectfully submit that recapitulating the discussion during the interview regarding the construction of matrix B will also be helpful to illustrate this point.

First, as shown in the Examples of the application, the polypeptide sequences are aligned on a programmed computer using a multiple sequence alignment program. The number of sequences in the alignment of Example 1 is eight (8) and these are identified by "j" marker values ranging from 1 to 8 (*e.g.*, SEQ 1, SEQ 2, *etc.*). The aligned sequences are placed one under each other vertically and each column corresponds to a position identified by a marker value (*e.g.*, "i" or "k"). In Example 1, the first position of each aligned sequence is called POSITION 0 or POS0.

Second, matrix A is constructed. Matrix A is a NxM matrix where N is the number of sequences (*e.g.*, vertical rows) and M is the number of positions (*e.g.*, columns) of the polypeptide sequences in this matrix. Then, the values for the cells in matrix A are determined. This is done, for example, by inspecting the first position (POS 0) of the first sequence (SEQ 1) which is an "S" (serine amino acid residue) and comparing it to the first position (POS 0) of the reference sequence which is also an "S[.]". These two positions are the same so the value "1" (*i.e.*, A2) for the POS 0, SEQ 1 cell in matrix A. Then an inspection is made of the second position (POS 1) of the first sequence (SEQ 1) which is a "R" (arginine amino acid residue) and a comparison is made to the second position (POS 1) of the reference sequence which is a "V" (valine amino acid residue). These two positions are not the same, because the second position of the first sequence is mutated, so the value "0" (*e.g.*, A1 in the claimed methods) is inserted in the POS 1, SEQ 1 cell in matrix A. This process is continued until the end of the first sequence (SEQ 1) after which the first row of cells for SEQ 1 in matrix A have all been assigned values of

"0" or "1[.]" This process is continued for each sequence until all cells in matrix A have been assigned values.

Third, matrix B is constructed. All that is needed to make the matrix B is matrix A. Matrix B is an MxM matrix. This means that the number of columns and the number of rows is the same because the value of M is equal to the number of positions in the polypeptide sequences analyzed in matrix A (*e.g.*, POS 0, POS 1 *etc.*). Matrix B is a symmetrical matrix (*e.g.*, $B_{i,k}=B_{k,i}$) such that one can fill just half of it (*i.g.*, the cell having coordinates POS X0, POS X1 will contain the same value as the cell having coordinates POS X1, POS X0). This is true because, if a position X0 does not mutate simultaneously in matrix A with the position X1, then the contrary is also true (*i.e.*, position X1 does not mutate simultaneously in the context of matrix A with the position X0).

Next, the values for the cells in matrix B are determined. This is done for each cell in matrix B corresponding to a pair of positions (*e.g.*, POS 0, POS 0; POS 0, POS 1; POS 2, POS 7; *etc.*) by inspecting each pair of adjacent cells for each sequence (consider here the discussion above regarding the recitation of "irrespective of the value of j ranging from 0 to N") in each "position" column in matrix A. For example, in the cell at position 2 and position 7 (*e.g.*, POS 2, POS 7) of matrix B the column called POS 2 in matrix A and the column called POS 7 in the matrix A are inspected. Then a comparison is made between the two positions for each sequence. This is done by comparing the two columns to each other and the adjacent cells as one proceeds vertically down the column.

For example, for the first sequence (SEQ 1) in the POS 2 column, there is a "1" in the POS 2 column and a "1" in the POS 7 column meaning both positions are not mutated simultaneously. For the second sequence (SEQ 2) in the POS 2 column, there is a "1" and there is a "0" in the POS 7 column meaning that position 7 is mutated but not position 2 (*i.e.*, no simultaneous mutation). If this comparison process is continued until the bottom of the POS 2 and POS 7 columns in matrix A are reached, one can find a sequence were POS 2 mutates at the same time as POS 7 (*i.e.*, one can find a "0" at the second position at the same time, meaning for the same sequence both POS 2 and POS 7 contain a "0"). This is SEQ 5. Thus, the conclusion is POS 2 and POS 7 can mutate together so that the value entered in the cell with coordinates POS 2, POS 7 in matrix B is a "0[.]"

An additional example is provided by comparing the POS 0 and POS 1 column in matrix A to generate the value for the cell having coordinates POS 0, POS 1 in matrix B. If one looks down the POS 0 and POS 1 columns in matrix A, it can be seen these two positions do not mutate together (*i.e.*, for each sequence "0" values in the POS 0 column are not adjacent to "0" values in the POS 1 column). For this reason one inserts a value of "1" in the cell having coordinates POS 0, POS 1 in matrix B. Continuing this comparison for each position column in matrix A permits the completion of matrix B.

Fourth, matrix C is constructed. All that is needed to make the matrix C is matrix A. Matrix C is an MxM matrix. This means, again, that the number of columns and the number of rows is the same because the value of M is equal to the number of positions in the polypeptide sequences analyzed in matrix A (*e.g.*, POS 0, POS 1 *etc.*). Matrix C is also a symmetrical matrix (*e.g.*, $C_{i,k}=C_{k,i}$) such that one can fill just half of it (*i.e.*, the cell having coordinates POS X0, POS X1 will contain the same value as the cell having coordinates POS X1, POS X0). This is, again, true because, if position X0 either mutates simultaneously, or does not mutate at all, in matrix A with the position X1, then the contrary is also true (*i.e.*, position X1 mutates simultaneously, or does not mutate at all, in the context of matrix A with the position X0). The diagonal of matrix C is not useful.

Next, the values for the cells in matrix C are determined. Again, this is done for each cell in matrix C corresponding to a pair of positions (*e.g.*, POS 6, POS 8 *etc.*) by inspecting each pair of adjacent cells for each sequence (consider here, again, the discussion above regarding the recitation of "irrespective of the value of j ranging from 0 to N") in each position in matrix A. For example, in the cell at position 6 and position 8 (*e.g.*, POS 6, POS 8) of matrix C the column called POS 6 in matrix A and the column called POS 8 in matrix A are inspected. Then a comparison is made between the two positions for each sequence. This is done by comparing the two columns to each other and the adjacent cells as one proceeds vertically down the column.

For example, for the first sequence (SEQ 1) in the POS 6 column, there is a "1" in the POS 6 column and a "1" in the POS 8 column meaning both positions are not simultaneously mutated. For the second sequence (SEQ 2) in the POS 6 column, there is a "1" in the POS 6 column and a "1" in the POS 8 column. This is also true for the third sequence (SEQ 3) in the POS 6 column and the POS 8 column. For the fourth sequence (SEQ 4) in the POS 6 column, there is a "0" in the POS 6 column and a "0" in the POS 8 column meaning both positions

mutated simultaneously. For the fifth sequence (SEQ 5) and sixth sequences (SEQ 6) in the POS 6 column, there is a "1" in the POS 6 column and a "1" in the POS 8 column. For the seventh sequence (SEQ 7) in the POS 6 column, there is a "0" in the POS 6 column and a "0" in the POS 8 column. For the eighth sequence (SEQ 8) in the POS 6 column, there is a "1" in the POS 6 column and a "1" in the POS 8 column. Thus, the conclusion is that POS 6 and POS 8 either simultaneously mutate, or do not mutate at all, so that the value entered in the cell with coordinates POS 6, POS 8 in matrix C is a "1[.]" The Applicants note that the remainder of matrix C is similarly constructed using such column wise comparisons, however for the sake of compact prosecution the entire construction of matrix C will not be discussed in detail here.

In view of the foregoing and the discussion during the interview, the Applicants respectfully submit that one of ordinary skill in the art can, in fact, construct the matrices of the claims without undue experimentation.

The Applicants respectfully request the withdrawal of the rejections of the claims as non-enabled under 35 USC §112, first paragraph.

Claims 2-5, 7-10, 20, 28 and 29 are rejected under 35 USC §112, first paragraph, as containing new matter. The Applicants will also assume, for the sake of compact prosecution, the Examiner intended to apply the rejections to Claim 33 - not withdrawn Claim 31.

Amended Claims 2-5, 7-10, 20, 28, 29 and 33 do not contain new matter under 35 USC §112, first paragraph. Claims 2-5, 7-10, 20, 28 and 29 are dependent on independent Claim 35 and include all of its recitations. Claim 33 is dependent on new independent Claim 34 and includes all of its recitations. Together, this means amended Claims 2-5, 7-10, 20, 28 and 29 recite the step of "a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program" while amended Claim 33 recites the step of "a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a CLUSTAL algorithm based multiple sequence alignment program[.]" This is consistent with the discussion during the interview and the Examiner's guidance. Furthermore, the Applicants note that, as discussed during the interview, paragraphs [0014], [0037]-[0048], [0035], [0036], [0043], [0059], [0069], [0071], [0080] and [0084] of the originally filed application support these recitations of the particular machine which is tied to the claimed methods. Thus, consistent with the Examiner's

guidance and the discussion during the interview, Claims 2-5, 7-10, 20, 28, 29 and 33 do not contain new matter under 35 USC §112, first paragraph.

The Applicants respectfully request the withdrawal of the rejections of the claims under 35 USC §112, first paragraph, as containing new matter.

Claims 2, 4, 5, 9-10, 28 and 29 are rejected as obvious under 35 USC §103(a) over the combination of Rose and Zhang.

Amended Claims 2, 4, 5, 9-10, 28 and 29 are not obvious under 35 USC §103(a) over the combination of Rose and Zhang. This is because amended Claims 2, 4, 5, 9-10, 28 and 29 are dependent on independent Claim 34 and include all of its recitations. As discussed during the interview and in the previous Response, the combination of Rose and Zhang fails to teach all the elements of Claim 34. This was acknowledged by the Examiner during the interview and in the Official Action. Thus, the rejection fails to establish amended Claims 2, 4, 5, 9-10, 28 and 29 are *prima facie* obvious under 35 USC §103(a) over the combination of Rose and Zhang.

The Applicants respectfully request the withdrawal of the rejection of Claims 2, 4, 5, 9-10, 28 and 29 as obvious under 35 USC §103(a) over the combination of Rose and Zhang.

Claim 3 is rejected as obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

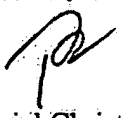
Amended Claim 3 is not obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins. This is because amended Claim 3 is dependent on independent Claim 35 and includes all of its recitations. As discussed during the interview and in the previous Response, the combination of Rose, Zhang and Collins fails to teach all the elements of new Claim 35. This was acknowledged by the Examiner during the interview and in the Official Action. Thus, the rejection fails to establish amended Claim 3 is *prima facie* obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

The Applicants respectfully request the withdrawal of the rejection of amended Claim 3 as obvious under 35 USC §103(a) over the combination of Rose, Zhang and Collins.

Claims 2-10, 20 and 28-29 have been provisionally rejected under 35 USC §101 as claiming the same invention as that of certain claims in the copending application having Serial No. 11/480,014. The Applicants respectfully request that the provisional double-patenting rejection made under 35 USC §101 be held in abeyance until the identification of allowable subject matter.

In light of the foregoing, the Applicants respectfully submit that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,



T. Daniel Christenbury
Reg. No. 31,750
Attorney for Applicants

TDC/vbm
(215) 656-3381